REMARKS

Claims 1-12 were pending in the application. In response to a Restriction Requirement, Applicants elected, with traverse, Group I, claims 1-6. Therefore claims 7-12 were withdrawn as belonging to a non-elected invention and are herein cancelled. Claims 1-5 are amended. The claim 1 amendment is supported at page 3, lines 4-6. The claim 5 amendment is supported at page 3, lines 16-23. The claims 2 and 3 amendments are supported by original claim 2. New claim 13 is supported by original claim 5.

The amendment to the specification corrects a typographical error and is supported by original claim 10.

The Office Action stated that the documents received with the IDS were considered but that documents not provided were not considered. Applicants note that this statement is directed to the publication of Carson et al., (1993) Circulation 87(6 Suppl):VI102-10, which is the only document not considered. This document was provided and can be found on PAIR as the first NPL Document listed for 04/26/2006, beginning on page 10 of that entry. However, for the Examiner's convenience, a copy of the reference is enclosed with this Response. Applicant requests that the reference be considered and that this be indicated by initialing a copy of the initial IDS, supplied.

35 USC § 112

Claims 1-6 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite for use of the acronym "ACE" instead of the full nomenclature. Claim 1 has been amended to correct the informality and Applicants request the rejection be reconsidered and withdrawn.

Claims 1-6 were rejected under 35 U.S.C. § 112, first paragraph, for nonenablement because the specification, while being enabling for a decrease in the incidence of symptomatic or asymptomatic left ventricular systolic dysfunction, is allegedly not enabling for total prevention of these dysfunctions. Claim 1, as amended, now recites that it is a method for reducing the incidence of atrial fibrillation. Applicants request the rejection be reconsidered and withdrawn.

35 USC § 102

Claims 1-6 were rejected under 35 U.S.C. 102(b) as being anticipated by Nicklas et al., NEJM, 1992, 327:685-691. Applicants traverse the rejection.

It is incumbent upon the Examiner to show that the prior art reference teaches each of the limitations of the claims, in order to support an anticipation rejection. In order to do so, the Examiner must discuss each of the limitations of the claims and show that each is taught in the reference. The Examiner has failed to do this and thus has not provided the *prima facie* showing of anticipation.

Claim 1 recites that the subject to whom the ACE inhibitor is administered has chronic heart failure. In contrast, the reference study discloses that the ACE inhibitor enalapril is administered to a subject with the object of *preventing the development of heart failure* (Abstract, first para.). To this end, the reference discloses administering enalapril to "patients who had no evidence of overt heart failure" (See: p. 385, Eligibility of Patients, Run-In Period, and Randomization). This is totally contrary to the claimed method which administers enalapril to a subject who has chronic heart failure.

Since the reference fails to teach all the limitations of the claims, the claims are novel over the cited art.

Claims 1-6 were rejected under 35 U.S.C. 102(b) as being anticipated by Soeki T. et al., (Jap. Heart J., 1998, 39(6):743-51). Applicants traverse the rejection.

Applicants protest that the Examiner asserts that she is rejecting the claims over the reference article but has supplied only the Abstract. Applicants clarify, for the record, that the rejection is based merely on the Abstract.

The Examiner has failed to discuss each of the limitations of the claims and has failed to show that each is taught in the Abstract. Thus, the Examiner has not provided a *prima facie* showing of anticipation.

Claim 1 is directed to a method for decreasing the incidence of atrial fibrillation in a subject with chronic heart failure by administration of an ACE inhibitor. The Soeki et al. Abstract provides no disclosure that enalapril administration decreases the incidence of atrial

fibrillation (AF) events. The Office Action relies on disclosure that in one subject, the cause of heart failure in the patient's earlier history was atrial fibrillation. However, that statement goes to the fact that there was atrial fibrillation before any enalapril was administered. The Abstract never states that the incidence of AF was studied after administering enalapril. Thus, the statement relied upon by the Examiner does not disclose that the reference disclosed the method of claim 1.

Still further, amended claim 2 recites that the chronic heart failure in the patient results from asymptomatic left ventricular systolic dysfunction (LVSD). The Abstract discloses causes of the chronic heart failure and does not disclose, among them, asymptomatic LVSD. Thus, claim 2 is, in yet another respect, novel over the Abstract.

Even further, new claim 13 recites that the ACE inhibitor is enalapril administered at a dosage of about 20 mg/day. The Soeki et al. Abstract does not disclose administration of enalapril at a dosage of 20 mg/day. Thus, claim 13 is, in yet another respect, novel over the Abstract.

For all the above reasons, Applicants assert that the claims are not anticipated by the cited references and request that the rejections be reconsidered and withdrawn.

35 USC § 103

Claims 1-6 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bourassa et al. (JACC, 1993, vol. 22, no. 4, pages 14A-19A) in view of Nicklas et al. Applicants traverse the rejection.

It is incumbent upon the Examiner to provide a "rational underpinning to support the legal conclusion of obviousness" as required by *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, __ (2007). However, the reasoning provided by the Examiner for combining the references lacks any rational underpinning and contains errors of fact.

The Office Action states, in error, that "Nicklas et al. teaches the use of enalapril to treat heart failure." (Off. Act. p. 10). As explained for the rejection above, Nicklas et al. does not treat patients with heart failure. Nicklas et al. discloses treating patients with no overt heart failure.

The Office Action further states that Bourassa et al. teach that an ACE inhibitor prevents heart failure and prolongs survival. Thus, the only commonality between these two teachings is

that ACE inhibitors, when administered *to persons without heart failure* can prevent heart failure. The Examiner discussed no teaching that predicts whether ACE inhibitors are beneficial if given to patients who have heart failure.

The error infects the Examiner's rationale for combining the references and leaves it with no rational basis. To wit, the Examiner's rationale was: "Given what is taught in Bourassa et al. there is a clear motivation in the prior art to administer an ACE inhibitor such as enalapril taught by Nicklas et al. to patients with heart failure or left ventricular dysfunction." This is incorrect. The Examiner has not discussed any motivation for administering an ACE inhibitor *to a patient with heart failure*. Thus the Examiner has not presented a *prima facie* showing of obviousness over any of the claims, which all require that the ACE inhibitor is administered to a patient with chronic heart failure.

Still further, as discussed above, claims 2 and 13 have additional limitations not taught in the references. For this reason as well, these claims are patentable over the cited art.

Secondary factors of unobviousness must also be considered when weighing whether an invention is patentable. One of these factors is a showing of unexpected results. In the present case, the inventive method provides that administration of an ACE inhibitor has a beneficial effect in terms of decreasing the incidence of atrial fibrillation in persons with chronic heart failure. This is unexpected, since the art had not predicted that ACE inhibitors affect incidence of atrial fibrillation by persons with chronic heart failure.

For all the above reasons, the claims are patentable over the cited art. Applicants request that the rejections be reconsidered and withdrawn.

In view of the foregoing, Applicants submit that all pending claims are in condition for allowance and request that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application.

It is believed that no fee is required. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,

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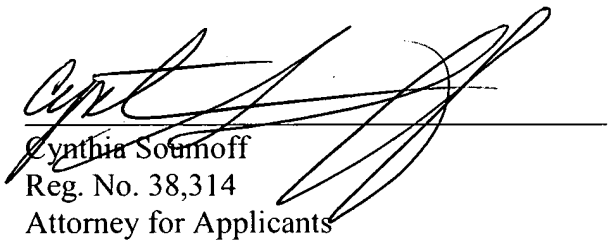

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